REMARKS

Reconsideration and allowance of the above-identified application are respectfully requested.

Claims 1, 2, 5, 8 – 38, 40, 41, and 46 are currently pending, wherein claim 1 is independent. Claims 1, 5, and 24 have been amended. Claims 3, 4, 6, 7, 39, and 42-45 have been cancelled, without prejudice or disclaimer. New claim 46 has been added. Support for new claim 46 can be found in the specification and in original claim 39.

On page 2 of the Office Action, claims 42 and 43 are objected to under 37 C.F.R. 1.75(c) as allegedly being of improper dependent form. Applicant respectfully notes that claims 42 and 43 have been cancelled. Accordingly, reconsideration and withdrawal of this objection are respectfully requested.

Rejection of claims under 35 U.S.C. § 112, second paragraph should be withdrawn

On page 3 of the Office Action, claims 5, 6, 24, and 39 stand rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. These rejections are respectfully traversed.

The rejection as it relates to claim 6 has been rendered moot in light of that claim's cancellation. The rejection has also been rendered moot as it relates to claim 5 by virtue of the fact that claim 5 has been amended to no longer recite the term "about." The rejection as it relates to claim 24 has been rendered moot by virtue of the fact that claim 24 has been amended to depend from claim 16 — a claim that recites, *inter alia*, the oral administration of both the opioid and the devazepide. Finally, the rejection as it relates to claim 39 has been rendered moot in light of that claim's cancellation. In light of the foregoing, Applicant

respectfully requests reconsideration and withdrawal of the rejection of claims 5, 6, 24, and 39 under 35 U.S.C. § 112, second paragraph.

Rejection of claims under 35 U.S.C. § 103(a) should be withdrawn

On page 5 of the Office Action, claims 1, 2, 5, 8, 9, 12 – 24, 27 – 32, 36-38, 40, and 41 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Panos *et al.* (Published PCT Appl. No. WO 99/18967, hereinafter "Panos") in view of Dourish *et al.* (*The Journal of Pharmacology and Experimental Therapeutics 255*: 1158-1164 (1990), hereinafter "Dourish"). In addition, claims 10, 11, 25, 26, and 33 – 35 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Panos and Dourish and further in view of U.S. Patent No. 6,103,261 to Chasin *et al.* (hereinafter "Chasin") and Caplan *et al.* (*JAMA 261*: 1036-1039 (1989), hereinafter "Caplan"). These rejections are respectfully traversed.

In an effort merely to facilitate prosecution in the present application and not for any purpose related to patentability, Applicant has amended independent claim 1 to recite that the opioid and devazepide are administered "regularly" and that the opioid dose required goes down or is reduced "over a period of at least 5 weeks." Support for such an amendment can be found in the present application at paragraph [0032], first sentence, and at paragraph [0034], second sentence. No new matter has been introduced by way of these amendments.

It is well settled that the Patent Office bears the burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103. *In re Deuel*, 51 F.3d 1552, 1557 (Fed. Cir. 1995); *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993). To establish a *prima facie* case of obviousness, the Patent Office must first show that the prior art suggested to those of ordinary skill in the art that they should make the claimed device or composition. Second, it

must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the Patent Office must show that the prior art teaches or suggests all the claim limitations. *Manual of Patent Examination and Procedure* (MPEP) § 2143; *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

These criteria must be satisfied with factual and objective evidence found in the prior art: an examiner's conclusory statement cannot form a basis for a *prima facie* case of obviousness. *In re Sang-Su Lee*, 277 F.3d 1338, 1343-4 (Fed. Cir. 2002). Thus, when conducting an analysis under 35 U.S.C. § 103(a), an Examiner "must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made." MPEP § 2142. This is important, as "impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art." *Id.* Consequently, when determining whether or not a claimed invention is obvious, one must cast his/her "mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then accepted wisdom in the field." *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999).

Applicants respectfully assert that the Patent Office has not met its burden for establishing a *prima facie* case of obviousness of the claims over the cited references for at least the reasons that follow. First, it is respectfully submitted that Panos does not teach or suggest that devazepide itself can act to enable the overall dose of the opioid to be reduced or minimized, concurrent with improved analgesia, *i.e.*, an increase in the analgesia, or a

lowering of "pain level," experienced by the patient. Further, it is respectfully submitted that Panos does not teach or suggest that devazepide acts as a synergist allowing both a reduction in the opioid dose while increasing the effect of the analgesic, *i.e.*, the level of pain goes down **accompanied** by the dose of opioid going down. Finally, it is respectfully submitted that Panos does not teach or suggest that the amount of opioid can be reduced by between about 25 to about 95% by weight, particularly when the opiod and devazepide are administered regularly and over a period of at least 5 weeks.

Instead, Panos teaches away from the claimed invention by teaching that a **fixed** dosage preparation of devazepide and an opioid is necessary in order to potentiate the analgesic effects of the opioid. Further, Panos teaches that devazepide has no intrinsic analgesic properties (page 1160, second column, second paragraph) and has no effect on tail withdrawal latencies in an animal model when given alone (abstract and page 1161, second column, last paragraph). Finally, Panos teaches that morphine analgesia is enhanced by devazepide when either is given as a single dose over a two hour test period. There are no data for long term or "regular" dosing or data showing that the observed effects are simply transient or if they are sustainable. It is respectfully submitted that there is simply no teaching or suggestion in Panos of the potential for devazepide to act as an adjuvant to morphine therapy in man, and that regularly administered devazepide would influence the specified reduction of between 25-95% by weight of the opioid dose required to achieve analgesia over the period of time recited in the claims. In short, Panos does not teach or suggest to those of ordinary skill in the art that they should make the claimed composition. Furthermore, the teachings of Dourish, Chasin or Caplan do not remedy the aforementioned deficiencies. Accordingly, Panos, alone or in combination with Dourish, Chasin and Caplan,

does not teach or suggests all the claim limitations, *viz.*, achieving the specified reduction of between 25-95% by weight of the opioid dose required to achieve analgesia or over the period of time recited in the claims when devazepide is administered regularly. In addition, Panos, alone or in combination with Dourish, Chasin and Caplan, does not provide one of ordinary skill in the art with a reasonable expectation of success in achieving the specified reduction of between 25-95% by weight of the opioid dose required to achieve analgesia over period of time recited in the claims when devazepide is administered regularly.

Therefore, it is respectfully submitted that Panos, alone or in combination with Dourish, Chasin and Caplan, does not render obvious the subject matter of independent claim 1.

Dependent claims 2, 5, 8, 9, 12 – 24, 27 – 32, 36-38, 40, 41, and 46 variously depend from independent claim 1, and are, therefore, patentably distinguishable over Panos, alone or in combination with Dourish, Chasin and Caplan, for at least those reasons stated above with regard to claim 1.

For at least the foregoing reasons, it is respectfully submitted that Panos, alone or in combination with Dourish, Chasin and Caplan, does not render the subject matter of claims 1, 2, 5, 8, 9, 12 – 24, 27 – 32, 36-38, 40, 41, and 46 unpatentable.

Accordingly, reconsideration and withdrawal of these grounds of rejection are respectfully requested.

All of the objections and rejections raised in the Office Action having been addressed, it is respectfully submitted that the present application is in condition for allowance and a notice to that effect is earnestly solicited. Should the Examiner have any questions regarding this amendment or the application in general, the Examiner is urged to contact the Applicant's attorney, Ricardo J. Moran, by telephone at (202) 625-3620. All correspondence should continue to be directed to the address given below.

Respectfully submitted,

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